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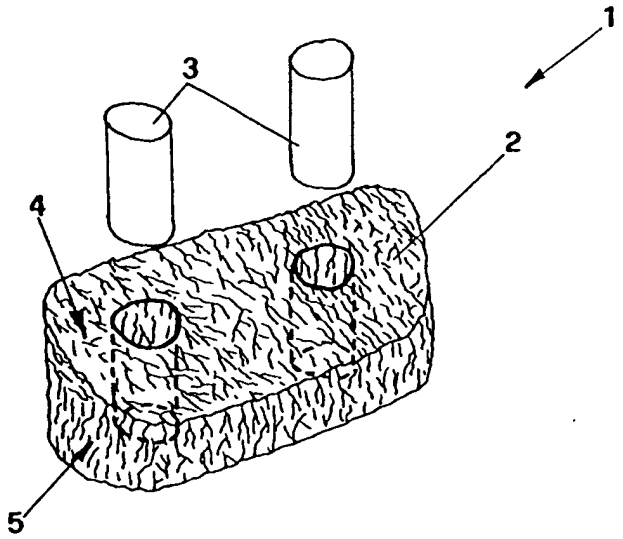
(54) Title: BIOMEDICAL GRAFT FOR SKELETAL STRUCTURES



(57) Abstract: A biomedical graft (1; 10) for skeletal structures particularly adapted to be inserted between bone members (V1; V2; V3; V4) subject to high load is disclosed, comprising a main portion (2; 11) which is inserted between said bone members (V1; V2; V3; V4) and a secondary insert portion (3; 12) which is inserted into the main portion (2; 11). The two portions (2; 3; 11; 12) have different characteristics of mechanical strength and at least one of the two portions consists of antigen free and reabsorbable bone tissue.

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BIOMEDICAL GRAFT FOR SKELETAL STRUCTURES

The present invention relates to a biomedical graft particularly adapted to be used in surgical operations for reconstruction of skeletal structure.

Reconstruction surgery techniques of parts of the skeletal structure are known, that are required for instance because of traumatic fracture of bones, pathologic forms such as tumors, osteoporosis or slipped disk and in tibial osteotomy surgery as well.

This kind of operations generally consists in inserting in the affected zones grafts that after surgery have the support function peculiar to bones or in other cases the spacing function as it happens for instance for intervertebral disks.

A first known surgery technique consists in replacing the injured bone portion with an autologous portion by removing and grafting suitable bone portions of the same patient or in other cases of a donor.

Such a method warrants a full reabsorption of the grafted bone by the receiving organism, with limited rejection problems because the graft is recognized as a part of the same organism.

A first problem of said method consists in that the portion of removed bone does not always have the characteristics of mechanical strength of the parts to be replaced, since the bony structure is different according to the kind of bone.

A second problem of this method is the need to carry out a preliminary surgery thus damaging the limb from which the portion is removed thus causing the inevitable post-operative troubles for the donor.

In order to avoid said inconveniences surgery methods were introduced that do not use autologous parts.

A first method belonging to the prior art consists in using a prosthesis with the main spacing function to keep constant distance between the bodies in which it is interposed.

More particularly as shown in fig. 1, this method is widely used in operations to replace injured intervertebral disks, for instance because of slipped disks.

These artificial prostheses generally consist of two shells of strong material, such as a chromium-cobalt alloy, inside which disks of plastic material are inserted, allowing by their elasticity the prosthesis to fit between the vertebras.

In other applications, couples of said prostheses are arranged fore and aft or aside the invertebral zone, so as to keep integrity of the central zone concerned by the spinal cord.

A limitation of said technique consists in that the prosthesis being made of inert material, constitutes a foreign body that cannot be absorbed by the organism thus remaining permanently in it.

Another inconvenience of said technique consists in that the inert material of the prosthesis does not allow formation of biological bond between the skeletal structure and the prosthesis but only a mechanical link.

Another known technique consists in using prostheses in the form of grids generally called "cage" according to the English terminology.

Said "cage" is generally formed by a cylindrical envelope with a cage-like structure of material of high compressive strength such as Titanium.

As the "cage" is internally empty, once it is grafted, it is filled with a proper material such as bone dust, promoting formation of the bony bridge between the graft zones.

In a first application of said technique shown schematically in fig. 2, the "cage" is anchored to the bones of two following cervical vertebras and subsequently filled with bone dust promoting formation of the bony bridge between said vertebras.

In a different application as shown in fig. 3 and for a different pathology, a couple of "cages" is arranged in a horizontal direction in the intervertebral zone and outside the medullary zone of two lumbar vertebras.

The main limitation of such technique consists, as for the previously described case, in that the material by which the "cage" is made is inert and therefore cannot be absorbed by the organism. Therefore the "cage" remains permanently inside the organism after operation with only a mechanical link and not a biological bond.

In order to overcome said problems, grafts could be used consisting of non inert biocompatible bony tissue allowing to obtain after application a permanent biological bond by formation of a bony bridge and the full substitution with time of the graft for the endogenous bone.

Indeed it is known that in the treatment for preparation of bony tissues for medical use, generally of animal origin, there is a first phase of removing any organic residue through solvents, and a second phase of removing any solvent trace through a process of ceramization making said tissue also inert.

To this purpose the same applicant developed a method of preparing bony tissues wherein the treatment for removing organic animal residues allows the

tissue to keep in any case the starting viable structure without being made inert.

At the end of the treatment in such a way a bone fragment is obtained, which is antigen free and totally reabsorbable by any organism in which it is grafted, more particularly the human body.

Bone fragments of sufficient size to make a graft can be obtained only by spongy bone tissues that are known to have good absorption characteristics but at the same time a low compressive strength.

On the other hand bone fragments with good compressive strength, for instance made of compact bone tissue, are contained in limited zones of the bones and do not allow to obtain grafts of sufficient size.

On the other hand the high resistance of the compact bone tissue arising from its structure decreases the tissue absorption ability in comparison with the spongy bone tissue.

The present invention aims at removing the above-mentioned drawbacks and overcoming the cited limitations concerning the treated bone tissues.

The main object of the invention is to provide a biomedical graft that can be highly absorbed by the organism in which it is grafted.

Another object of the invention is to provide a biomedical graft having a high mechanical strength adapted to resist the high loads to which the skeletal structure is subject.

A further object of the invention is to provide a graft made using spongy bone tissue.

Another object of the invention is to provide a graft allowing to be absorbed in a short time relative to the prior art solutions.

Said objects and others that will be cited in the following description, are attained by a biomedical graft for skeletal structures particularly adapted to be inserted between bone members subject to high load, that according to the contents of the main claim, is characterized by comprising at least a main portion inserted between said bone members and at least a secondary portion to be inserted in said main portion, said portions having different characteristics of mechanical strength, at least one of said portions consisting of antigen free and reabsorbable bone tissue.

According to a preferred embodiment the main portion has a generally disk-like shape consisting of antigen free spongy bone tissue.

Between the upper and lower surface defining said disk, the secondary insert portions are transversally arranged, made of antigen free and reabsorbable compact bone tissue having high characteristics of mechanical strength.

In a different embodiment the main portion consists of antigen free and reabsorbable compact bone tissue of generally cylindrical shape and the secondary insert portions are arranged perpendicularly to the main portion and are made with spongy tissue.

Further characteristics and features of the invention will be better understood by reading the following description of two preferred embodiments of the invention given as a non limiting illustrative example and shown in the accompanying sheets of drawings in which:

- Figs. 1 to 3 show different constructional versions of the prior art;
- Fig. 4 is an isometric exploded view of the graft of the invention;
- Fig. 5 is a side view of fig. 4;
- Fig. 6 shows an executive variation of fig. 4;
- Fig. 7 is a side view of fig. 6;
- Fig. 8 shows an application of the device of fig. 4;
- Fig. 9 shows an application of the device of fig. 6; and
- Fig. 10 shows a further application of the device of fig. 4.

The graft of the invention is shown in figs. 4 and 5 where it is generally indicated with reference numeral 1.

The graft comprises a main portion 2 in which the secondary insert portions 3 are inserted, shown in fig. 4 separated from the main portion 2 for sake of simplicity, but inserted inside the main portion 2 in the final assembly.

More particularly as shown in fig. 4, the main portion 2 has a generally disk-like shape defined by the upper plain surface 4 and the lower plain surface 5, said surfaces belonging to corresponding mutually converging planes giving to the graft 1 a wedge-like shape.

The secondary insert portions 3 are developed transversally to surfaces 4 and 5, being two in this embodiment, of generally cylindrical shape and defining a main axis X as shown in fig. 5.

In this embodiment the main portion 2 preferably consists of antigen free and reabsorbable spongy bone tissue while the secondary insert portions 3 are of the compact type.

Fig. 6 shows an executive variation of the graft of fig. 1 and is generally

indicated with numeral 10.

In this embodiment the main portion 11 has a generally cylindrical shape and is developed along axis Y. This portion preferably consists of antigen free and reabsorbable compact bone tissue.

Along the body defined by the main portion 11 two secondary insert portions 12 are inserted having a generally cylindrical shape, whose axes Z are arranged along a direction perpendicular to axis Y along which the main portion 11 is developed, and consist of antigen free and reabsorbable spongy bone tissue.

An application of the graft 1 of the invention is shown in fig. 8 concerning operations of reconstruction of intervertebral cortical bodies of the spinal cord.

In this application a couple of grafts 1 of the invention is arranged between two vertebras V1, V2 of the backbone, a first graft 1 being positioned before the central zone M concerning the spinal cord and the other graft behind it.

More particularly one can see that the axis X defined by the secondary insert portions 3 is coincident with the load direction along which the backbone is stressed by the body weight.

The function of mechanical resistance to stress is carried out by the secondary insert portions 3 that being made of compact bone tissue, have a high mechanical strength.

The main portion 2 preferably made of spongy bone tissue, promotes absorption of graft 1 of the invention in the post operative phase by the organism so as to reach the intersomatic fusion between the two vertebras V1, V2.

In fig. 9 the application of the graft 10 of fig. 6 is shown in the particular case of intervertebral application for cervical vertebras.

In this illustration a couple of grafts 10 is positioned in the intervertebral zone defined between the two vertebras V3, V4 and arranged laterally relative to the central zone M concerning the spinal cord.

More particularly as the main portion 11 consists of compact bone tissue, it is the same main portion carrying out the function of mechanical strength between the vertebras V3, V4.

The two secondary insert portions 12 of spongy bone tissue arranged with their axis Z intersecting the vertebras V3, V4, promote obtainment of the bony bridge between them and therefore the intersomatic fusion.

The application of such a kind of grafts 10 will be advantageous as in the just described case, where the required dimensions are small and allow to make the main portion 11 with compact bone tissue that is present in the bones only in zones of limited size.

Fig. 10 shows the application of the graft 1 of the invention in case of operations of tibial-osteotomy wherein the graft 1 of the invention has the general function of shimming wedge between the zones in which it is inserted.

The secondary insert portions 3 carry out the function of load resistance along the direction X coincident with the direction of the load to which the tibial bone is subject, while the main portion 2 allows formation of the bony bridge.

The graft of the invention may also be used advantageously generally in applications not shown in the drawings for recovery of damaged bones that are not subject to a high load.

With reference to the described applications, after the operation between the graft and the bone structure in which it is inserted, a permanent biological bond is obtained rather quickly, both for the main portion and the secondary insert portions, with consequent formation of the bony bridge ensuring its early stabilization.

From the foregoing it is clear that the biomedical graft of the invention attains the intended objects through its embodiments.

In an executive phase further modifications neither described nor shown in the accompanying sheets of drawings may be made to the graft of the invention.

Such modifications may for instance consist of different shape of the main portion and of the secondary insert portion, a different number and arrangement of the secondary insert portions or a different material by which they are made, such as Titanium, ceramics or other biomaterial with high resistance.

It is however to be understood that these and other modifications when falling within the inventive conception set forth in the appended claims, are to be considered covered by the present patent.

CLAIMS

1) A biomedical graft (1; 10) for skeletal structures particularly adapted to be inserted between bone members (V1; V2; V3; V4) subject to high load, **characterized by** comprising at least a main portion (2; 11) that is inserted between said bone members (V1; V2; V3; V4) and at least a secondary insert portion (3; 12) which is inserted in said main portion (2; 11), said portions (2; 3; 11; 12) having different characteristics of mechanical resistance, at least one of said portions being made of antigen free and reabsorbable bone tissue.

2) The graft (1) according to claim 1 **characterized in that** said at least a main portion (2) consists of said antigen free and reabsorbable bone tissue of the spongy type adapted to promote intersomatic fusion of said bone members (V1; V2).

3) The graft (1) according to claim 2 **characterized in that** said at least a secondary insert portion (3) consists of said antigen free bone tissue of compact type arranged along the direction (X) defined by said load and adapted to carry out the mechanical strength between said bone members (V1; V2).

4) The graft (1) according to claim 2 **characterized in that** said at least a secondary insert portion (3) consists of inert material with high mechanical resistance arranged along the direction (X) defined by said load and adapted to carry out the mechanical strength between said bone members (V1; V2).

5) The graft (1) according to claim 4 **characterized in that** said inert material is titanium.

6) The graft (1) according to claim 4 **characterized in that** said inert material consists of bioceramics.

7) The graft (1) according to claim 4 **characterized in that** said inert material consists of biomaterial.

8) The graft (1) according to claim 1 **characterized in that** said at least a main portion (2) has a generally disk-like shape defined by two facing surfaces (4; 5) said at least a secondary insert portion (3) having a generally cylindrical shape being developed transversally to said surfaces.

9) The graft (1) according to claim 8 **characterized in that** said facing surfaces (4; 5) belong to corresponding mutually convergent planes adapted to give to said graft (1) a generally wedge-like shape.

10) The graft (10) according to claim 1 **characterized in that** said at least a

main portion (11) consists of said antigen free and reabsorbable bone tissue of the compact type adapted to carry out the mechanical strength between said bone members (V3; V4).

11) The graft (10) according to claim 10 **characterized in that** said at least secondary insert portion (12) consists of said antigen free bone tissue of the spongy type adapted to promote the intersomatic fusion of said bone members (V3; V4).

12) The graft (10) according to claim 11 **characterized in that** said at least a main portion (11) has a generally cylindrical shape, said at least a secondary insert portion (12) has a generally cylindrical shape, the axis (Y) of said at least a main portion (11) and the axis (Z) of said at least a secondary insert portion (12) being generally perpendicular to each other.

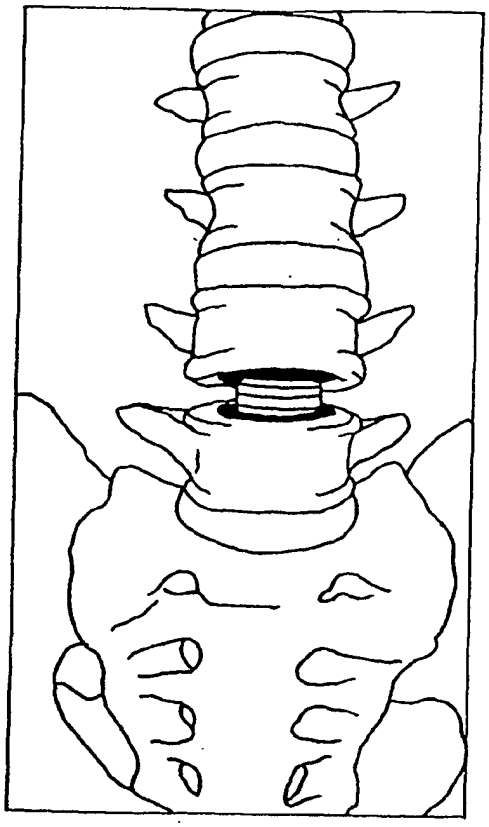

FIG.1 PRIOR ART

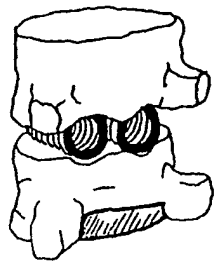

FIG.3 PRIOR ART

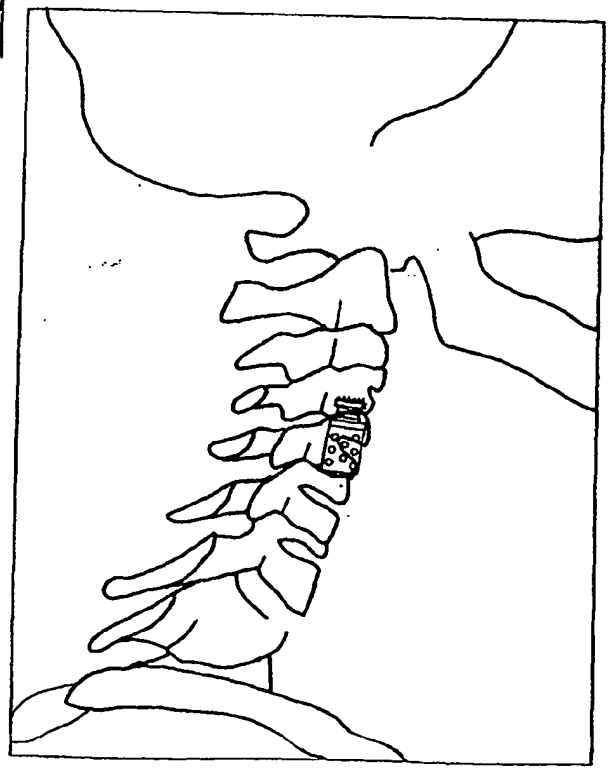

FIG.2
PRIOR ART

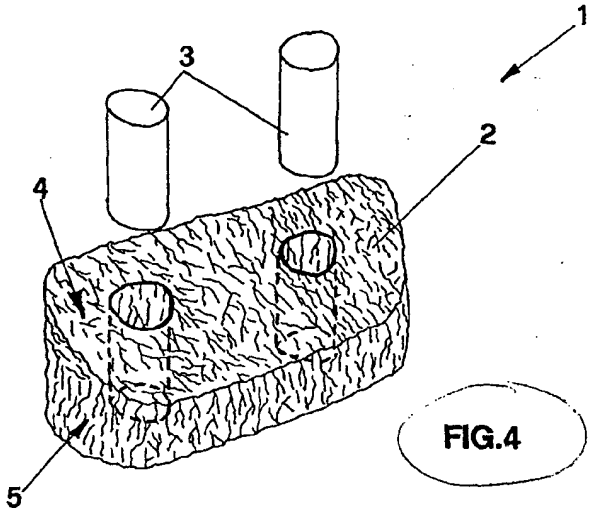

FIG.4

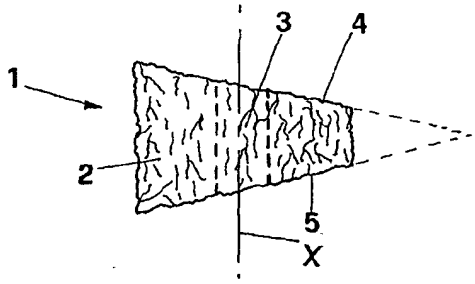

FIG.5

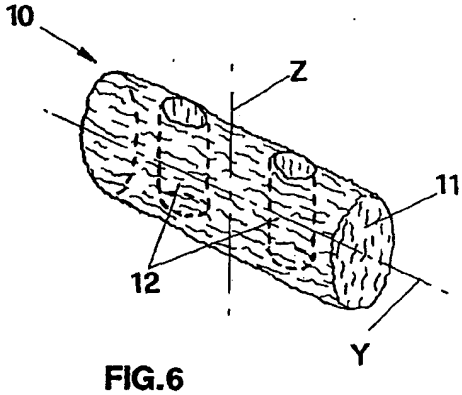

FIG.6

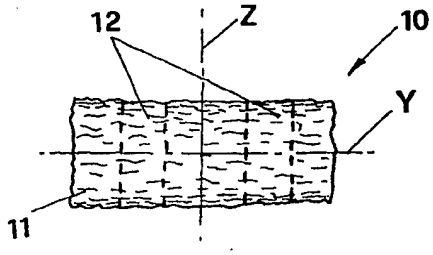

FIG.7

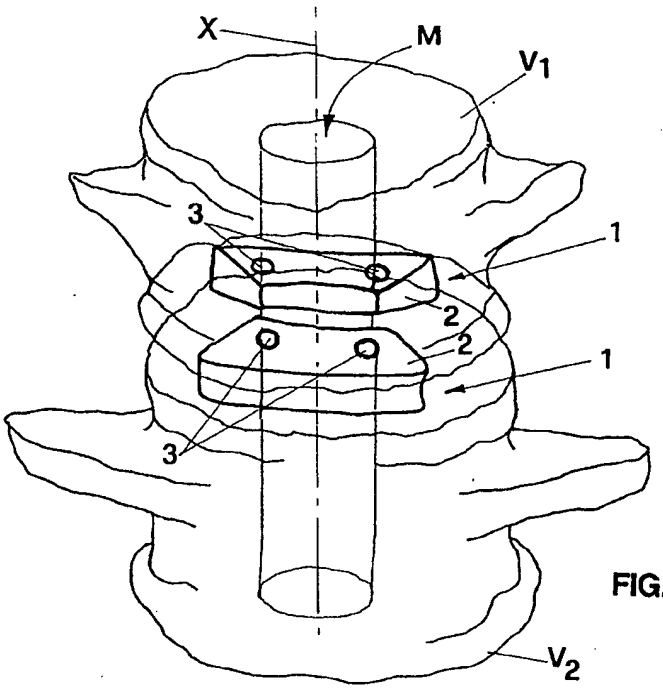

FIG.8

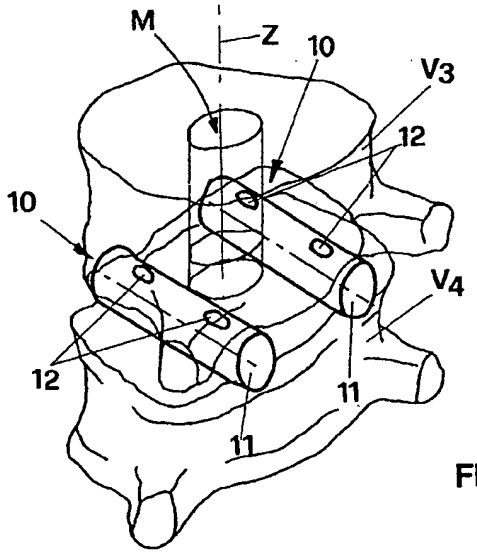

FIG.9

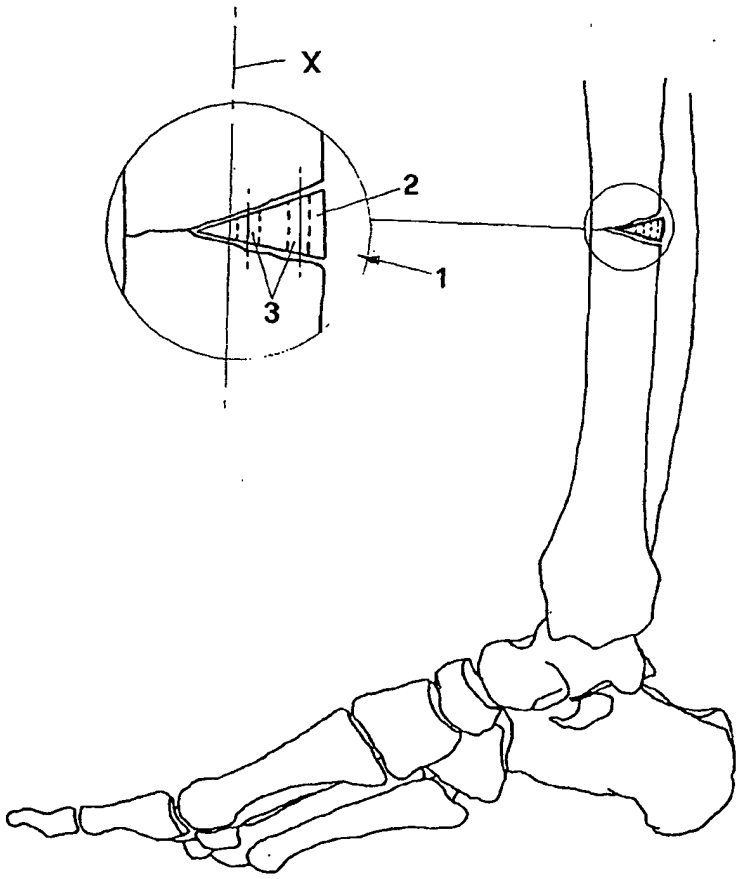

FIG.10

INTERNATIONAL SEARCH REPORT

International Application No
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A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61F2/28 A61F2/44

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 41654 A (SDGI HOLDINGS INC ;BOYD LAWRENCE M (US); DORCHAK JOHN D (US); BURK) 20 July 2000 (2000-07-20) claims 1-5,8-10; figure 9 page 3, line 16 - line 19 page 16, line 3 - line 16 page 21, line 25 - line 27 page 24, line 29 -page 25, line 12 ---	1-7, 10-12
X	WO 98 17209 A (HOECK JAMES E VAN ;SDGI HOLDINGS INC (US); BOYD LAWRENCE M (US); M) 30 April 1998 (1998-04-30) claims 56-59; figures 24-33,38-49 page 19, line 18 - line 26 page 25, line 34 -page 26, line 11 --- -/--	1,8, 10-12

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

* Special categories of cited documents :

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Date of the actual completion of the international search	Date of mailing of the international search report
22 October 2002	29/10/2002

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Stach, R

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INTERNATIONAL SEARCH REPORT

International Application No
PCT/EP 02/05996

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4 950 296 A (MCINTYRE JONATHAN L) 21 August 1990 (1990-08-21) claims 1,9; figures ---	1,8, 10-12
X	WO 01 08714 A (REGENERATION TECHNOLOGIES INC) 8 February 2001 (2001-02-08) figures 4-8; examples 1,9,13 page 22, line 1 -page 24, line 17 ---	1,10-12
X	US 6 200 347 B1 (WOLFINBARGER JR LLOYD ET AL) 13 March 2001 (2001-03-13) figures 35A,35B column 24, line 9 - line 35 ---	1,8,9
X	US 5 769 897 A (HAERLE ANTON) 23 June 1998 (1998-06-23) claims 1-3,11-13,16; figures 1-10	1,8,9
A	---	5-7
A	FR 2 741 525 A (VOYDEVILLE GILLES) 30 May 1997 (1997-05-30) ---	
P,X	US 2001/039457 A1 (ANGELUCCI CHRISTOPHER M ET AL) 8 November 2001 (2001-11-08) claims 22-25; figure 18 column 8, paragraph 3 -----	1-3

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/EP 02/05996

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0041654 A	20-07-2000	AU 2499500 A	01-08-2000
		AU 2963300 A	01-08-2000
		EP 1143885 A2	17-10-2001
		EP 1139930 A2	10-10-2001
		WO 0041654 A2	20-07-2000
		WO 0041655 A2	20-07-2000
WO 9817209 A	30-04-1998	AU 732421 B2	26-04-2001
		AU 4994697 A	15-05-1998
		EP 0955961 A2	17-11-1999
		JP 2000507484 T	20-06-2000
		WO 9817209 A2	30-04-1998
		US 6371988 B1	16-04-2002
		US 5989289 A	23-11-1999
		US 5888222 A	30-03-1999
US 4950296 A	21-08-1990	NONE	
WO 0108714 A	08-02-2001	AU 6499800 A	19-02-2001
		EP 1202755 A1	08-05-2002
		WO 0108714 A1	08-02-2001
US 6200347 B1	13-03-2001	EP 1148847 A1	31-10-2001
		WO 0040177 A1	13-07-2000
		US 6458158 B1	01-10-2002
US 5769897 A	23-06-1998	NONE	
FR 2741525 A	30-05-1997	FR 2741525 A1	30-05-1997
US 2001039457 A1	08-11-2001	AU 4936701 A	03-10-2001
		AU 4936801 A	03-10-2001
		AU 4936901 A	03-10-2001
		WO 0170139 A2	27-09-2001
		WO 0170136 A2	27-09-2001
		WO 0170137 A2	27-09-2001
		US 2001039456 A1	08-11-2001
		US 2001056302 A1	27-12-2001
		US 2001039458 A1	08-11-2001
		US 2001041941 A1	15-11-2001